IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
LIVSHITS et al.	Art Unit: 1656
Application No.: 09/466,935	Examiner: David J. STEADMAN
Filing Date: December 20, 1999	Attorney Ref. No.: US-126O
For: NOVEL GENE AND METHOD FOR PRODUCING L-AMINO ACIDS	Confirmation No.: 1750

BRIEF FOR APPELLANT

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
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Sir:

COMES NOW the Appellant to present this Brief in support of the appeal of the final rejections of Claims 77-84 in the above-captioned patent application. The Notice of Appeal was timely filed on 13 September 2007 with a Petition with a two-month extension of time, and a Request for a Pre-Appeal Brief Conference Request. The Notice of Panel Decision from Pre-Appeal Brief Review was issued on October 19, 2007, maintaining the rejections and resetting the time period for filing an Appeal Brief to one-month from the date of the Notice. As this Appeal Brief is filed on or before November 19, 2007, this Brief is timely filed.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. If, however, additional extensions of time are necessary to prevent abandonment of this application or dismissal of this appeal, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is hereby authorized to charge fees necessitated by this paper, and to credit all refunds and overpayments, to the credit card authorized on the attached PTO-2038.

For the following reasons, Appellant respectfully submits that the final rejection of each of Claims 77-84 in this application is in error, and therefore respectfully requests reversal of the rejections.

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I. Real Party in Interest

The real party in interest is Ajinomoto Co., Inc, a corporation of Japan.

II. Related Appeals and Interferences

There are no related appeals or interferences.

III. Status of Claims

Claims 1-76 are cancelled. Claims 77-84 are pending and appealed. No claims are in condition for allowance. Claims 77-84 stand finally rejected in the Office Action dated 16 April 2007, and are on appeal.

IV. Status of Amendments

All amendments to the claims have been entered.

V. Summary of Claimed Subject Matter

Claim 77: A method of producing an L-amino acid comprising A) cultivating in a culture medium a bacterium transformed with a DNA that encodes a protein comprising the amino acid sequence of SEQ ID NO: 4, B) removing solids including cells from the medium; and C) purifying said L-amino acid from the medium obtained in step B). (see specification, page 8, lines 6-12, page 14, line 15 - page 16, line 8, page 21, line 8 – page 23, line 7).

VI. Grounds of Rejection to Be Reviewed on Appeal

A. Whether Claims 77-84 are unpatentable under 35 U.S.C. § 102(b) as being anticipated by Kobayashi et al. as evidenced by Zakataeva et al and Kruse et al..

B. Whether Claims 77-84 are unpatentable under 35 U.S.C. § 103(a) over Kobayashi et al. in view of Georgiou et al. as evidenced by Zakataeva et al. and Kruse et al..

VII. Argument

A. Legal Standard – 35 U.S.C. §102

Claim construction begins with the words of the claims. *Karlin Tech., Inc. v. Surgical Dynamics, Inc.*, 177 F.3d 968, 971 (Fed. Cir. 1999). Claim language should be interpreted as one reasonably skilled in the art would have interpreted the claim at the time of the patent application date. *Vivid Techs., Inc. v. American Science & Engineering, Inc.*, 200 F.3d 795, 804 (Fed. Cir. 1999); *Wiener v. NEC Elec., Inc.*, 102 F.3d 534, 539 (Fed. Cir. 1996). Where the claim term has no specialized meaning to persons of skill in the art, the ordinary meaning of the words to those of ordinary skill in the art controls, unless the evidence indicates that the inventor used them differently. *Karlin*, 177 F.3d at 971. Such evidence includes the specification and prosecution history, both of which must be analyzed to determine if the inventor limited or redefined any of those terms. *Watts v. XL Sys., Inc.*, 232 F.3d 877, 882-84 (Fed. Cir. 2000); *Vivid Techs.*, 200 F.3d at 804. If claim language is not clear on its face, then intrinsic evidence also should be consulted to resolve the lack of clarity. *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001).

Under the doctrine of anticipation, a patent claim is not patentable if the claimed invention lacks novelty. 35 U.S.C. § 102(b); *Karsten Mfg. Comp v. Cleveland Golf*, 242 F.3d 1376, 1383 (Fed. Cir. 2001). Anticipation, a question of fact, focuses on a comparison of the prior art to the subject matter of the claim at issue. *Celeritas Technologies, Ltd. v. Rockwell International Corp.* 150 F.3d 1354, 1361 (Fed. Cir. 1998). "[A] claim is anticipated if each and every limitation is found either expressly or inherently in a single prior art reference." *Celeritas*, 150 F.3d at 1361. A convenient way to consider anticipation is the "four corners" doctrine. The "four corners" doctrine refers to the idea that anticipation requires that each and every limitation of the claimed invention is described either expressly or inherently within the four corners of a single prior art document. *Advanced Display Systems, Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000).

B. Legal Standard – 35 U.S.C. §103

Claimed subject matter is obvious in light of the prior art if it would have been obvious to one of ordinary skill in the relevant art at the time the invention was made. 35 U.S.C. § 103(a). In considering the entire prior art in the relevant field, the claimed subject matter is obvious if the prior art "would have suggested to one of ordinary skill in the art that this [invention should be made] and would have a reasonable likelihood of success." *In re Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988).

Obviousness can be shown either directly by demonstrating the technical motivation to combine the prior art, *Life Technologies, Inc. v. Clontech Laboratories, Inc.*, 224 F.3d 1320, 1326 (Fed. Cir. 2000), by showing that there existed at the time of the invention a known problem for which there was an obvious solution, *KSR International Co. v. Teleflex Inc. et al.*, No. 04-1350, slip op. at 16 (S.Ct., April 30, 2007), or indirectly through "secondary considerations" after the claimed subject matter was invented, *Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc.*, 807 F.2d 955, 960 (Fed. Cir. 1986). However, neither the patentee's particular motivation for making the invention, nor their avowed purpose, controls. *KSR, slip op.* at 17. To show a motivation to combine prior art, it is not enough to simply identify different references that might be combined in hindsight; showing obviousness may be accomplished by showing a motivation to combine the pieces (*Velander v. Garner*, 348 F.3d 1359, 1363 (Fed. Cir. 2003)) or showing a combination of familiar elements according to known methods which yields no more than predictable results. *KSR,* slip op. at 12. That motivation or reason might come from a reference or from the knowledge of an artisan of ordinary skill. The level of ordinary skill in an art is based on a number of factors, including the educational level of the inventor, the type of problems encountered in the art, prior solutions to those problems, and the speed of innovation in the art. *Ruiz v. A.B. Chance Co.*, 234 F.3d 654, 666-67 (Fed. Cir. 2000).

The U.S. Supreme Court has very recently addressed the obviousness of a combination of known elements. Although a rigid application of the Court of Appeals for the Federal Circuit's "teaching, suggestion, or motivation" test was rejected, the Court stated that "a combination of

familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR, slip op.* at 12. For example, the Court explained, when the prior art elements work together in an unexpected and fruitful manner, a finding of non-obviousness is supported. *Id.* (*citing United States v. Adams,* 383 U.S. 39, 40 (1966)). If, however, the combination of old elements does no more than they would in separate, sequential operation, even though the combination might perform a useful function, the combination is likely non-obvious. *Id.* at 13 (*citing Anderson's-Black Rock, Inc. v. Pavement Salvage Co.,* 396 U.S. 57 (1969)). Finally, the Court stated that "[i]f a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability." *Id.* (*citing Sakraida v. AG Pro, Inc.,* 425 U.S. 273 (1976)).

"Secondary considerations" focus on how the invention was received in the market; a very successful or surprising invention is probably not obvious. *See Custom Accessories, Inc.*, 807 F.2d at 960. The "secondary considerations" considered by the courts include: commercial success, copying of the invention by others, licensing of the invention, evidence of a long-felt need for the invention, skepticism by skilled artisans that the claimed invention could be achieved, prior failures of others to achieve the same result, and unexpected results. *Id.*; *Pentec, Inc. v. Graphic Controls Corp.*, 776 F.2d 309, 316 (Fed. Cir. 1985). No secondary consideration is required for an invention to be non-obvious, but a court may use evidence of secondary considerations in its determination of obviousness (or non-obviousness). *Custom Accessories, Inc.*, 807 F.2d at 960.

C. The rejection of Claims 77-84 under 35 U.S.C. § 102(b)is in error

Claims 77-84 were rejected under 35 U.S.C. § 102(b), as reciting subject matters that allegedly are anticipated by Kobayashi et al. (hereinafter, "Kobayashi"), as evidenced by Zakataeva et al. (hereinafter, "Zakataeva") and Kruse et al. (hereinafter, "Kruse"). Appellant respectfully requests reconsideration of this rejection.

The claims are drawn to a method of producing an L-amino acid by 3 distinct, manipulative steps. That is, step 1 is cultivating the bacterium, step 2 is removing solids

including cells from the medium, and step 3 is purifying the L-amino acid from the medium obtained in step 2. These are distinct steps as indicated in the claim, for example, that the L-amino acid is purified from the medium obtained in the second step. Clearly, one cannot purify the L-amino acid recited in step 3 without first obtaining the medium in step 2, that is, a medium having the solids, including cells, removed. Contrary to the teachings of any of the cited references, the desired product, the L-amino acid, is purified from the supernatent, that is the medium, after removing solids, including cells, from the medium. This is explicitly stated in the claims, in that step B states that the solids, such as the cells and cellular debris, are removed from the culture medium, and step C states that the L-amino acid is purified from the medium obtained in step B). It is undisputed that this medium is the supernatent obtained after removing the cells and cellular debris.

It is asserted that the Examiner has made an error in interpreting the claims, and as a result, has mis-applied the prior art. Specifically, Kobayashi is cited for teaching an *E. coli* host cell transformed with vector pAB104, which comprises a DNA segment which includes the region between and including genes pldA and pldB (see p. 1012, figure 4 and p. 1014, figure 6). This region includes the DNA of SEQ ID NO: 3, which encodes the amino acid sequence of SEQ ID NO: 4, as demonstrated by Zakataeva. Appellants have agreed with this interpretation of these references. Kruse is cited to show that *E. coli* is an L-threonine-producing strain. However, Kobayashi fails to teach the recovery or purification of an L-amino acid, nor even any indication that an L-amino acid might be present in the medium following the cultivation and centrifugation of the cultivated cells, and the evidentiary references fail to make up for this deficiency.

Specifically, the Examiner has cited to the teaching in Kobayashi, on page 1009 in the section entitled "Enzyme Assay" at the bottom of column 1, that the strain harboring the desired vector is cultured, and then the cells are 'spun down' and washed. The pellet, which contains the solids such as the cells and cellular debris, was further processed and the objective enzymes were further purified from the processed pellet. The medium is not used for any purpose and is likely discarded, as it is NOT further processed. There is no disclosure of recovering any substance

from the medium or supernatent that remains after the 'spinning'. There is no disclosure that any substance ***could be*** isolated from the medium or supernatent. More importantly, the reference of Kobayashi fails to teach, either explicitly or implicitly, step C of claim 1, that is, the purification of the L-amino acid from the medium obtained in step B.

The Examiner has stated that "by practicing the method of Kobayashi, one of ordinary skill in the art would be "removing solids" in accordance with step B and purifying said L-amino acid" in accordance with step C simultaneously." (see page 3 of the Office Action mailed April 16, 2007). The Examiner explains that the step of centrifuging the cells would simultaneously remove solids from the medium and purify the L-amino acid, which is in the cells, from the medium. This interpretation of the prior art and application to the claims is a clear error. This is because the claims distinctly recite 3 manipulative steps, that is, cultivating the bacterium, removing solids including cells from the medium, and purifying the L-amino acid ***from the medium*** obtained in the second step. These are distinct steps as indicated in the claim, for example, that the L-amino acid is purified from the medium obtained in the second step. Clearly, one cannot purify the L-amino acid without first obtaining the medium in the second step, that is, a medium having the solids, including cells, removed. The Examiner has erred in interpreting steps B and C to be combined into one. It is clear that step C cannot be conducted without first obtaining the medium from step B. It is impossible to combine them for this reason. Merely separating the pellet with the cellular debris from the medium cannot be interpreted as "purifying the L-amino acid ***from the medium"***, as the medium is only obtained as a result of this separation.

Furthermore, Kobayashi teaches away from purifying L-amino acids from any cell culture since the only description of a culture method describes manipulation of the post-centrifugation pellet, which does not contain the objective L-amino acids. The term "purifying" as defined in the specification on page 23, lines 2-7 clearly indicates a manipulative step such as "ion exchange, concentration and crystalline fraction methods..." is performed, which is not described or suggested by the Enzyme Assay of Kobayashi. This represents a further clear error in the interpretation of the claim, as the Examiner has refused to read the claims' terms in light of

the specification. Although it is acknowledged that the purification methods decribed in the specification at page 23 cannot be imported into the claim, Appellant's definition cannot be completely ignored. The Examiner is completely ignoring this definition in the specification, as it clearly indicates that the claim must be interpreted to actually indicate a purification of the amino acid from the medium, not merely separating a medium from a pellet, as is taught by Kobayashi.

In summary, Kobayashi fails to teach step (C) of claim 77. The standard for anticipation has been clearly set forth in the case law, specifically, "[A] claim is anticipated if each and every limitation is found either expressly or inherently in a single prior art reference." *Celeritas Technologies, Ltd. v. Rockwell International Corp.* 150 F.3d 1354, 1361 (Fed. Cir. 1998). The courts have provided further guidance in the "four corners" doctrine. The "four corners" doctrine refers to the idea that anticipation requires that each and every limitation of the claimed invention is described either expressly or inherently within the four corners of a single prior art document. *Advanced Display Systems, Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000). Clearly, Kobayashi has failed to meet this standard, and the evidentiary references fail to overcome this fact.

For at least the foregoing reasons, Appellant respectfully submits that the subject matters of Claims 77-84 are not anticipated by Kobayashi, Zakataeva, and Kruse, and are therefore not unpatentable under 35 U.S.C. § 102, and therefore Appellant respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 102.

D. The rejection of Claims 77-84 under 35 U.S.C. § 103(a)is in error

Claims 77-84 were rejected under 35 U.S.C. § 103(a), as reciting subject matters that allegedly are obvious over Kobayashi in view of Georgiou et al. (hereinafter, "Georgiou"), as evidenced by Zakataeva and Kruse. Appellant respectfully requests reconsideration of this rejection.

This rejection was first made in the Final Office Action of April 16, 2007, and is applied

"in view of an alternative interpretation of amended claim 77". (see page 4 of the April 16, 2007 Office Action). The Georgiou reference allegedly teaches a method of determining the growth phase of E. coli by measuring the optical density. To take this measurement, one takes an aliquot during growth. The Examiner asserts it would have been obvious to one of ordinary skill in the art to combine the teachings of Kobayashi and Georgiou to culture the host cell of Kobayashi, and remove an aliquot of the culture for optical density measurement in order to determine when the cells reached mid-exponential growth phase. The Examiner then states that once the aliquot is taken, one would know to centrifuge the cells and prepare a cell extract of the harvested cells.

As Kobayashi, Zakataeva, and Kruse were discussed above, the teachings of Georgiou in combination with these references is only discussed *infra.* The application of Georgiou to the claims does not overcome the shortcomings of Kobayashi, in that there is still no teaching of purifying an amino acid from the aliquot or the medium after removing the solids from the medium. Furthermore, one of ordinary skill must have a reason or motivation to combine the references (*KSR International Co. v. Teleflex Inc. et al.,* No. 04-1350, slip op. at 16 (S.Ct., April 30, 2007)), and there is no commonality in the teachings of these references that would provide a reason for the person of ordinary skill in the art to combine these teachings. Neither reference has the goal of producing an L-amino acid, nor discuss such production in reference to the methods taught. As neither reference teaches or suggests such a method or even the desire to obtain an L-amino acid, the methods taught by these references fail to render obvious the claimed method. There is no teaching in any of the 4 cited references of step C in the claimed method, nor any suggestion from the various teachings of centrifugation of the various cultures, including the step of removing an aliquot in Georgiou. Therefore, this reference adds nothing to the rejection and fails to anticipate or render obvious the claimed invention.

For at least the foregoing reasons, Appellant respectfully submits that the subject matters of Claims 77-84 are not obvious over Kobayashi in view of Georgiou, as evidenced by Zakataeva and Kruse, and are therefore not unpatentable under 35 U.S.C. § 103, and therefore Appellant respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 103.

VIII. Conclusion

For at least the foregoing reasons, Appellant respectfully submits that the subject matters of Claims 77-84, each taken as a whole, are patentable. Accordingly, Appellant respectfully requests reversal of the rejections of Claims 77-84 under sections 102(b) and 103(a).

Respectfully submitted,

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APPENDIX A: CLAIMS ON APPEAL

77. A method of producing an L-amino acid comprising

A) cultivating in a culture medium a bacterium transformed with a DNA that encodes a protein comprising the amino acid sequence of SEQ ID NO: 4,

B) removing solids including cells from the medium; and

C) purifying said L-amino acid from the medium obtained in step B).

78. The method of claim 77, wherein

said DNA comprises the nucleotide sequence of nucleotides 187 to 804 of SEQ ID NO: 3.

79. The method of claim 77, wherein the bacterium is further transformed with a second DNA that encodes a protein comprising the amino acid sequence of SEQ ID NO: 2.

80. The method of claim 79, wherein said second DNA comprises the nucleotide sequence of nucleotides 557 to 1171 of SEQ ID NO: 1.

81. The method of claim 77, wherein said L-amino acid is L-threonine.

82. The method of claim 78, wherein said L-amino acid is L-threonine.

83. The method of claim 79, wherein said L-amino acid is L-threonine.

84. The method of claim 80, wherein said L-amino acid is L-threonine.

APPENDIX B: EVIDENCE

None.

APPENDIX C: RELATED PROCEEDINGS

None.